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IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

APPLICATION NO. 10/736,087	FILING DATE 12/15/2003	FIRST NAMED INVENTOR Joseph C. Walsh	ATTORNEY DOCKET NO. 2003P88074US
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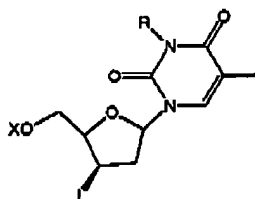
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AMENDMENTS TO THE CLAIMS

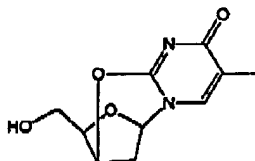
In the Claims, please make the following amendments:

1. (Withdrawn) A method of preparing an ^{18}F -FLT precursor having the following formula:



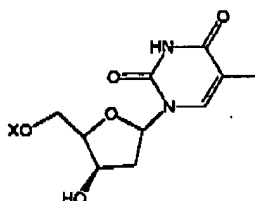
wherein X is t-butoxycarbonyl, methyl, methoxymethyl ethyl, isobutyl, tetrahydropyranyl ether, tetrahydrofuranyl ether, methoxymethyl ether, bis-(2-chloroethoxy)methyl ether, 1-ethoxyethyl ether, or 1-methyl-1-methoxyethyl ether; P is an amine protecting group; and L is a leaving group, comprising the steps of:

- a. reacting a compound having the following formula:



with a reagent that opens the 2,3'-anhydro ring to produce 3'-beta-hydroxy thymidine;

- b. protecting the 5'hydroxyl group to produce a compound having the following formula:



wherein X is the same as defined above;

- c. incorporating a leaving group at the 3'-position to produce a compound having the following formula:

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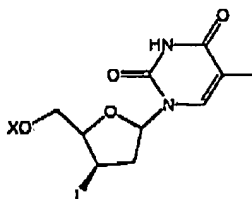
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wherein X and L are the same as defined above; and

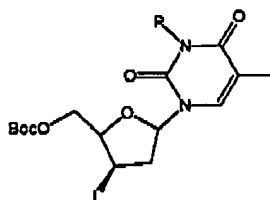
- d. protecting the 3-N amine moiety to produce the precursor.
2. (Withdrawn) The method according to Claim 1, wherein the amine protecting group is selected from the group consisting of tert-butoxycarbamate, isopropyl carbamate, pivaloyloxymethyl carbamate, methyl carbamate, allyl carbamate, N-tetrahydropyran, N-tetrahydrofuran; t-butylamide, and N-pyrrolidinomethylamide.
3. (Withdrawn) The method according to Claim 1, wherein the amine protecting group is t-butoxycarbonyl.
4. (Withdrawn) The method according to Claim 1, wherein X is t-butoxycarbonyl, methyl, methoxymethyl ethyl, or isobutyl.
5. (Withdrawn) The method according to Claim 1, wherein X is t-butoxycarbonyl.
6. (Withdrawn) The method according to Claim 1, wherein L is selected from the group consisting of benzenesulfonyl, methylsulfonyl, p-methylbenzenesulfonyl, 4-nitrobenzene sulfonyl, p-bromobenzenesulfonyl, trifluoromethylsulfonyl, trichloroacetimidate, 2,2,2-trifluoroethanesulfonyl, and imidazolesulfonyl.
7. (Withdrawn) The method according to Claim 1, wherein L is nosylate.
8. (Withdrawn) The method according to Claim 1, wherein the precursor is 5'-O-Boc-3'-β-nosyl-3-N-Boc thymidine.
9. (Withdrawn) The method according to Claim 1, wherein the 2,3'-anhydro ring is opened by reacting 2,3'-anhydrothymidine with NaOH, KOH, LiOH, or tetrabutylammonium hydroxide.
10. (Withdrawn) A method of preparing an ¹⁸F-FLT precursor having the following formula:

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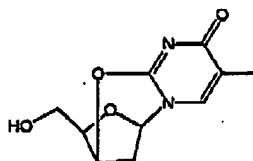
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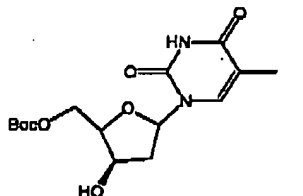
wherein P is an amine protecting group and L is a leaving group, comprising the steps of:

- a. reacting a compound having the following formula:

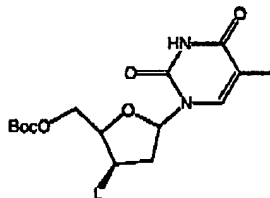


with a reagent that opens the 2,3'-anhydro ring to produce 3'-beta-hydroxy thymidine;

- b. reacting the reaction product of step (a) with BOC_2O to produce a compound having the following formula:



- c. incorporating a leaving group at the 3'-position to produce a compound having the following formula:



wherein L is the same as defined above; and

- d. protecting the 3-N amine moiety to produce the precursor.

11. (Withdrawn) The method according to Claim 10, wherein the amine protecting group is selected from the group consisting of tert-butoxycarbamate, isopropyl

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carbamate, pivaloyloxymethyl carbamate, methyl carbamate, allyl carbamate, *N*-tetrahydropyran, *N*-tetrahydrofuran; *t*-butylamide, and *N*-pyrrolidinomethylamide.

12. (Withdrawn) The method according to Claim 10, wherein the amine protecting group is *t*-butoxycarbonyl.

13. (Withdrawn) The method according to Claim 10, wherein L is selected from the group consisting of benzenesulfonyl, methylsulfonyl, *p*-methylbenzenesulfonyl, 4-nitrobenzene sulfonyl, *p*-bromobenzenesulfonyl, trifluoromethylsulfonyl, trichloroacetimidate, 2,2,2-trifluoroethanesulfonyl, and imidazolesulfonyl.

14. (Withdrawn) The method according to Claim 10, wherein L is nosylate.

15. (Withdrawn) The method according to Claim 10, wherein the precursor is 5'-*O*-Boc-3'- β -nosyl-2-*N*-Boc thymidine.

16. (Withdrawn) The method according to Claim 10, wherein the 2,3'-anhydro ring is opened by reacting 2,3'-anhydrothymidine with NaOH, KOH, LiOH, alkylammonium hydroxides such as tetrabutylammonium hydroxide.

17. (Withdrawn) A method for preparing an ^{18}F -FLT precursor comprising:

- converting thymidine into 2,3'-anhydrothymidine;
- opening the 2,3'-anhydro ring to produce 3'-beta-hydroxy thymidine;
- protecting the 5'-hydroxy with *t*-butoxycarbonyl;
- incorporating a leaving group at the 3'-position; and
- protecting the 3-N amine to produce the precursor.

18. (Withdrawn) A method according to Claim 17, wherein the 2,3'-anhydro ring is opened by reacting 2,3'-anhydrothymidine with NaOH, KOH, LiOH, or tetrabutylammonium hydroxide.

19. (Withdrawn) A method according to Claim 17, wherein the 5'-hydroxy is protected by reacting the reaction product of step (b) with BOC_2O .

20. (Withdrawn) A method according to Claim 17, wherein the leaving group is a sulfonate ester.

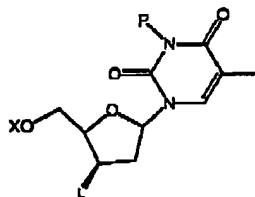
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21. (Withdrawn) A method according to Claim 17, wherein L is selected from the group consisting of benzenesulfonyl, methylsulfonyl, p-methylbenzenesulfonyl, 4-nitrobenzene sulfonyl, p-bromobenzenesulfonyl, trifluoromethylsulfonyl, trichloroacetimidate, 2,2,2-trifluoroethanesulfonyl, and imidazolesulfonyl.
22. (Withdrawn) A method according to Claim 17, wherein L is nosylate, tosylate, or mesylate.
23. (Withdrawn) A method according to Claim 17, wherein the amine protecting group is selected from the group consisting of tert-butoxycarbamate, isopropyl carbamate, pivaloyloxymethyl carbamate, methyl carbamate, allyl carbamate, *N*-tetrahydropyran, *N*-tetrahydrofuran; t-butylamide, and *N*-pyrrolidinomethylamide.
24. (Withdrawn) A method according to Claim 17, wherein the amine protecting group is t-butoxycarbonyl.
25. (Withdrawn) A compound having the following formula:



wherein X is t-butoxycarbonyl, methyl, methoxymethyl ethyl, isobutyl, tetrahydropyranyl ether, tetrahydrofuran ether, methoxymethyl ether, bis-(2-chloroethoxy)methyl ether, 1-ethoxyethyl ether, or 1-methyl-1-methoxyethyl ether; P is an amine protecting group; and L is a leaving group.

26. (Withdrawn) A compound according to Claim 25, wherein P is selected from the group consisting of tert-butoxycarbamate, isopropyl carbamate, pivaloyloxymethyl carbamate, methyl carbamate, allyl carbamate, *N*-tetrahydropyran, *N*-tetrahydrofuran; t-butylamide, and *N*-pyrrolidinomethylamide.
27. (Withdrawn) A compound according to Claim 25, wherein P is t-butoxycarbonyl.
28. (Withdrawn) A compound according to Claim 25, wherein L is a sulfonate ester.

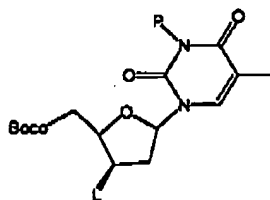
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29. (Withdrawn) A compound according to Claim 25, wherein L is selected from the group consisting of benzenesulfonyl, methylsulfonyl, p-methylbenzenesulfonyl, 4-nitrobenzene sulfonyl, p-bromobenzenesulfonyl, trifluoromethylsulfonyl, trichloroacetimidate, 2,2,2-trifluoroethanesulfonyl, and imidazolesulfonyl.
30. (Withdrawn) A compound according to Claim 25, wherein L is nosylate, tosylate, or mesylate
31. (Withdrawn) A compound according to Claim 25, wherein X is t-butoxycarbonyl, methyl, methoxymethyl ethyl, or isobutyl.
32. (Withdrawn) A compound having the following formula:



wherein P is an amine protecting group and L is a leaving group.

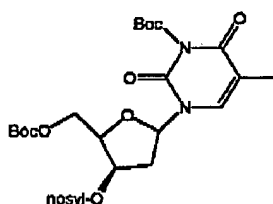
33. (Withdrawn) A compound according to Claim 32, wherein P is selected from the group consisting of tert-butoxycarbamate, isopropyl carbamate, pivaloyloxymethyl carbamate, methyl carbamate, allyl carbamate, *N*-tetrahydropyran, *N*-tetrahydrofuran; *t*-butylamide, and *N*-pyrrolidinomethylamide.
34. (Withdrawn) A compound according to Claim 32, wherein P is t-butoxycarbonyl.
35. (Withdrawn) A compound according to Claim 32, wherein L is a sulfonate ester.
36. (Withdrawn) A compound according to Claim 32, wherein L is selected from the group consisting of benzenesulfonyl, methylsulfonyl, p-methylbenzenesulfonyl, 4-nitrobenzene sulfonyl, p-bromobenzenesulfonyl, trifluoromethylsulfonyl, trichloroacetimidate, 2,2,2-trifluoroethanesulfonyl, and imidazolesulfonyl.
37. (Withdrawn) A compound according to Claim 32, wherein L is nosylate, tosylate, or mesylate.
38. (Withdrawn) A compound having the following formula:

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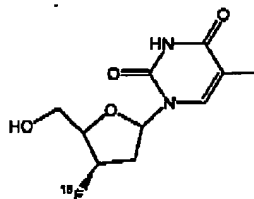
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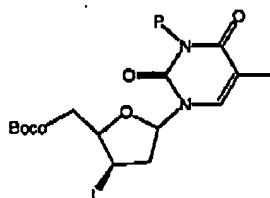


39. (Currently amended) A method for preparing a compound having the following formula:



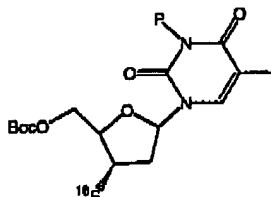
comprising:

a. [^{18}F]fluorinating a compound having the following formula:



wherein P is an amine protecting group and L is a leaving group, to produce a compound having the formula:

~~compound having the following formula:~~



wherein P is the same as defined above; and

b. removing the amine protecting group and Boc group to produce ^{18}F -FLT.

40. (Previously presented) A method according to Claim 39, wherein P is selected from the group consisting of tert-butoxycarbamate, isopropyl carbamate,

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pivaloyloxymethyl, carbamate, methyl carbamate, allyl carbamate, *N*-tetrahydropyran, *N*-tetrahydrofuran; *t*-butylamide, and *N*-pyrrolidinomethylamide.

41. (Previously presented) A method according to Claim 39, wherein P is *t*-butoxycarbonyl.
42. (Previously presented) A method according to Claim 39, wherein L is benzenesulfonyl, methylsulfonyl, *p*-methylbenzenesulfonyl, 4-nitrobenzene sulfonyl, *p*-bromobenzenesulfonyl, trifluoromethylsulfonyl, trichloroacetimidate, 2,2,2-trifluoroethanesulfonyl, or imidazolesulfonyl.
43. (Previously presented) A method according to Claim 39, wherein L is nosylate, tosylate, or mesylate.
44. (Previously presented) A method according to Claim 39, wherein P is *t*-butoxycarbonyl and L is nosylate.
45. (Previously presented) A method according to Claim 39, wherein the amine protecting group and boc groups are removed by acid hydrolysis.
46. (Previously presented) A method according to Claim 39, wherein the amine protecting group and boc group are removed by treating the reaction product of step (a) with HCl, HBr, HOAc, H₂SO₄, HI, trimethylsilyliodide, or H₃PO₄.
47. (Withdrawn) A method for preparing a precursor for the preparation of a radiolabeled nucleoside comprising:
- converting a 2'-deoxy nucleoside into a 2,3'-anhydronucleoside;
 - opening the 2,3'-anhydro ring to produce 3'-beta-hydroxy nucleoside;
 - protecting the 5'-hydroxy with *t*-butoxycarbonyl;
 - incorporating a leaving group at the 3'-position; and
 - protecting the 3-*N* amine to produce the radiolabeled nucleoside precursor.
48. (Withdrawn) The method according to Claim 47, wherein the nucleoside is thymidine, cytidine, or uridine.

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49. (Withdrawn) The method according to Claim 47, wherein the leaving group is nosylate, tosylate, or mesylate.

50. (Withdrawn) The method according to Claim 47, wherein the amine protecting group is t-butoxycarbonyl.

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